more type of cells selected from the group consisting of Madin-Darby bovine kidney (MDBK) cells, Madin-Darbu canine kidney (MDCK) cells and Vero cells.

3. (Amended) [A] The virus [as claimed in] of claim **Error! Reference source not found.**, wherein said virus [which] exhibits at least about one log reduction in plaque titre compared to the parent wild-type virus on MDBK cells.

4. (Amended) [A] The virus [as claimed in] of claim **Error! Reference source not found.** [or claim 3 which], wherein said virus exhibits at least about a 3 to 4 log reduction in plaque titre compared to the parent wild-type virus on MDCK cells and Vero cells.

5. (Amended) [A] The virus [as claimed in any one] of claim[s] 1 [to 4], wherein said genomic nucleic acid segment is a mutated native influenza virus genomic RNA segment.

6. (Amended) The [A] virus [as claimed in any one] of claim 1 or [to] 5 [which is], wherein said virus is an attenuated influenza virus of type A and [wherein] said nucleic acid segment is a mutated influenza A virus genomic RNA segment having [the] a mutation C to A at position 11 from the 3'-terminus of the native parent segment and [the] a mutation G to U at position 12' from the 5'-terminus of the native parent segment, or functionally equivalent substitutions at the same positions, so as to provide an attenuating base-pair substitution in the non-coding duplex region.

7. (Amended) [A] The virus [as claimed in] of claim 6, wherein said nucleic acid segment further comprises a [also has the] mutation U to G at position 10 from the 3' terminus of the native parent segment and [the] a mutation A to C at position 11' from the 5' terminus of the native parent segment, or functionally equivalent substitutions at the same positions, so as to provide an additional base-pair substitution in the non-coding duplex region.

8. (Amended) [A] The virus [as claimed in claim 6] of [or] claim 7 wherein said nucleic acid segment encodes neuraminidase (NA) or a functional modification thereof.

9. (Amended) [A] The virus [as claimed in any one of claims 1 to 8] of claim 1, [which] wherein said virus is a wild-type virus which has been attenuated by said base-pair substitution(s).

10. (Amended) [A] The virus[as claimed in any one of claims 1 to 8] of claim 1 [which additionally comprises] further comprising a heterologous coding sequence capable of being expressed in target cells.

11. (Amended) [A] The virus[as claimed in] of claim 10, wherein said heterologous coding sequence encodes an antigenic peptide or polypeptide capable [to] of stimulating an immune response to a pathogenic agent.

12. (Amended) [A] The virus[as claimed in] of claim 9, wherein said wild-type virus [which] is an attenuated influenza A/WSN/33 having a NA-encoding nucleic acid segment or a functional modification thereof [as defined in claim 8].

13. (Amended) A nucleic acid sequence comprising a genomic nucleic acid segment which comprises 5' and 3' non-coding regions providing a mutated duplex region of an influenza virus RNA genomic segment operably-linked to a protein coding sequence for an influenza viral protein or a functional modification thereof of said protein, wherein said duplex region is a non-chimeric duplex region, but has at least one base-pair substitution such that expression of said protein-coding sequence in cells infected by said virus is reduced to give an attenuated phenotype[as defined in claim 1 or any one of claims 5 to 8].

14. (Amended) The nucleic acid sequence of claim 13, wherein said sequence is a DNA sequence capable of transcription to provide a RNA sequence [a the nucleic acid sequence [according to of claim 13].

15. (Amended) A plasmid [containing] comprising the [a] DNA sequence of [as claimed in] claim 14.

16. (Amended) A ribonucleoprotein (RNP) complex [wherein] comprising [a] the nucleic acid [as claimed in] of claim 13 [is] complexed with polymerase proteins and nucleoprotein

of an influenza virus. [for use in preparing an attenuated virus as claimed in any one of claims 1 to 12]

17. (Amended) An *ex vivo* cell infected by a virus comprising a genomic nucleic acid segment which comprises 5' and 3' non-coding regions providing a mutated duplex region of an influenza virus RNA genomic segment operably-linked to a protein coding sequence for an influenza viral protein or a functional modification thereof of said protein, wherein said duplex region is a non-chimeric duplex region, but has at least one base-pair substitution such that expression of said protein-coding sequence in cells infected by said virus is reduced to give an attenuated phenotype.

18. (Amended) A vaccine comprising comprising a genomic nucleic acid segment which comprises 5' and 3' non-coding regions providing a mutated duplex region of an influenza virus RNA genomic segment operably-linked to a protein coding sequence for an influenza viral protein or a functional modification thereof of said protein, wherein said duplex region is a non-chimeric duplex region, but has at least one base-pair substitution such that expression of said protein-coding sequence in cells infected by said virus is reduced to give an attenuated phenotype.

19. (Amended) The vaccine [as claimed in] of claim 18 [which] further comprising [comprises a virus as claimed in claim 11 and which is capable of stimulating an immune response to an influenza virus and] a second pathogenic agent other than an influenza virus.

20. (Amended) A pharmaceutical composition comprising [a] the virus [as claimed in] of claim 10 in combination with a pharmaceutically acceptable carrier or diluent for delivery of said heterologous coding sequence to target cells.

21. (Amended) A pharmaceutical composition comprising cells infected with [a] the virus [according to] of claim 10 [or claim 11] in combination with a pharmaceutically acceptable carrier or diluent.

22. (Amended) A method of preparing a virus [according to any one of claims 1 to 12 which comprises] comprising the steps of:

constructing a genomic nucleic acid segment which comprises 5' and 3' non-coding regions providing a mutated duplex region of an influenza virus RNA genomic segment operably-linked to a protein coding sequence for an influenza viral protein or a functional modification thereof of said protein, wherein said duplex region is a non-chimeric duplex region, but has at least one base-pair substitution such that expression of said protein-coding sequence in cells infected by said virus is reduced to give an attenuated phenotype;

providing [in] to a host cell the genomic nucleic acid segments for said virus under conditions whereby said segments are packaged into a viral particle; and

selecting said virus.

23. (Amended) A method of [Use of a] preparing an attenuated influenza virus by a helper virus based influenza gene rescue system [as claimed in any one of claims 1 to 12] comprising the steps of:

transfecting a host cell with a helper virus, wherein said helper virus is an attenuated influenza virus comprising a genomic nucleic acid segment which comprises 5' and 3' non-coding regions providing a mutated duplex region of an influenza virus RNA genomic segment operably-linked to a protein coding sequence for an influenza viral protein or a functional modification thereof of said protein, wherein said duplex region is a non-chimeric duplex region, but has at least one base-pair substitution such that expression of said protein-coding sequence in cells infected by said virus is reduced to give an attenuated phenotype [as a helper virus to rescue an influenza virus genomic nucleic acid segment in cells,];

transfecting said host cell with a nucleic acid segment of an influenza virus to be resuced, wherein said host cell contains said helper virus; and

selecting [wherein] viruses [produced] containing said nucleic acid segment [are selected] on the basis of increased growth compared with the helper virus on cells of a selected type.

24. (Amended) The method of [Use of an influenza A virus as claimed in claim 8 as a helper virus in accordance with] claim 23, wherein said genomic nucleic acid segment and said nucleic acid segment encode neuraminidase [to rescue an NA encoding influenza A virus genomic nucleic acid segment] or a functional modification thereof.

25. (Amended) The method [Use as claimed in] of claim 24, wherein said helper virus is attenuated influenza A/WSN/33 having mutations C to A at position 11 from the 3'-terminus of the native parent segment and a mutation G to U at position 12' from the 5'-terminus of the native parent segment and mutations U to G at position 10 from the 3' terminus of the native parent segment and a mutation A to C at position 11' from the 5' terminus of the native parent segment [as and defined in claim 7 in the NA-encoding genomic RNA segment], and said host cell is [wherein selection of viruses carrying the nucleic acid segment to be rescued is carried out on] a Vero cell[s].

26. (Amended) A method of stimulating an immune response against an influenza virus, optionally together with stimulation of an immune response against one or more [further] pathogenic agents, [which comprises] comprising the step of administering to an animal in an [immunising] immunizing mode [an] the attenuated influenza virus [as claimed in any one] of claim[s] 1[to 11].

27. (Amended) A method of [delivery] delivering a heterologous coding sequence to cells [which comprises] comprising infecting said cells with [a] the virus [according to] of claim 10 [carrying said sequence.]

Please add the following new claims.

28. The method of claim 23, wherein said nucleic acid segment of an influenza virus is complexed with polyerase proteins and nucleoproteins to form a RNA complex which is transfected.

29. The nucleic acid sequence of claim 13, wherein said genomic nucleic acid segment is a mutated native influenza virus genomic RNA segment.

30. The nucleic acid sequence of claims 13, wherein said nucleic acid segment is a mutated influenza A virus genomic RNA segment having a mutation C to A at position 11

from the 3'-terminus of the native parent segment and a mutation G to U at position 12' from the 5'-terminus of the native parent segment, or functionally equivalent substitutions at the same positions, so as to provide an attenuating base-pair substitution in the non-coding duplex region.

31. The nucleic acid sequence of claim 30, wherein said nucleic acid segment further comprises a mutation U to G at position 10 from the 3' terminus of the native parent segment and a mutation A to C at position 11' from the 5' terminus of the native parent segment, or functionally equivalent substitutions at the same positions, so as to provide an additional base-pair substitution in the non-coding duplex region.

32. The nucleic acid sequence of claim 31, wherein said nucleic acid segment encodes neuraminidase (NA) or a functional modification thereof.

33. The *ex vivo* cell of claim 17, wherein said genomic nucleic acid segment is a mutated native influenza virus genomic RNA segment.

34. The *ex vivo* cell of claims 17, wherein said virus is an attenuated influenza virus of type A and said nucleic acid segment is a mutated influenza A virus genomic RNA segment having a mutation C to A at position 11 from the 3'-terminus of the native parent segment and a mutation G to U at position 12' from the 5'-terminus of the native parent segment, or functionally equivalent substitutions at the same positions, so as to provide an attenuating base-pair substitution in the non-coding duplex region.

35. The *ex vivo* cell of claim 34, wherein said nucleic acid segment further comprises a mutation U to G at position 10 from the 3' terminus of the native parent segment and a mutation A to C at position 11' from the 5' terminus of the native parent segment, or functionally equivalent substitutions at the same positions, so as to provide an additional base-pair substitution in the non-coding duplex region.

36. The *ex vivo* cell of claim 35, wherein said nucleic acid segment encodes neuraminidase (NA) or a functional modification thereof.

37. The *ex vivo* cell of claim 17, wherein said virus is a wild-type virus which has been attenuated by said base-pair substitution(s).

38. The *ex vivo* cell of claim 17 further comprising a heterologous coding sequence capable of being expressed in target cells.

39. The *ex vivo* cell of claim 38, wherein said heterologous coding sequence encodes an antigenic peptide or polypeptide capable of stimulating an immune response to a pathogenic agent.

40. The *ex vivo* cell of claim 37, wherein said wild-type virus is an attenuated influenza A/WSN/33 having a NA-encoding nucleic acid segment or a functional modification thereof.

41. The method of claim 22 or 23, wherein said helper virus is an attenuated influenza virus of type A and said genomic nucleic acid segment is a mutated influenza A virus genomic RNA segment having a mutation C to A at position 11 from the 3'-terminus of the native parent segment and a mutation G to U at position 12' from the 5'-terminus of the native parent segment, or functionally equivalent substitutions at the same positions, so as to provide an attenuating base-pair substitution in the non-coding duplex region.

42. The method of claim 41, wherein said genomic nucleic acid segment further comprises a mutation U to G at position 10 from the 3' terminus of the native parent segment and a mutation A to C at position 11' from the 5' terminus of the native parent segment, or functionally equivalent substitutions at the same positions, so as to provide an additional base-pair substitution in the non-coding duplex region.

43. The method of claim 22 or 23, wherein said helper virus is a wild-type virus which has been attenuated by said base-pair substitution(s).

44. The method of claim 22 or 23, wherein said helper virus further comprises a heterologous coding sequence capable of being expressed in target cells.

45. The method of claim 44, wherein said heterologous coding sequence encodes an antigenic peptide or polypeptide capable of stimulating an immune response to a pathogenic agent.

46. The method of claim 43, wherein said wild-type virus is an attenuated influenza A/WSN/33 having a NA-encoding nucleic acid segment or a functional modification thereof.

47. A helper virus comprising an attenuated influenza virus, wherein said virus comprises a genomic nucleic acid segment which comprises 5' and 3' non-coding regions providing a mutated duplex region of an influenza virus RNA genomic segment operably-linked to a protein coding sequence for an influenza viral protein or a functional modification thereof of said protein, wherein said duplex region is a non-chimeric duplex region, but has at least one base-pair substitution such that expression of said protein-coding sequence in cells infected by said virus is reduced to give an attenuated phenotype.

REMARKS

Entry of the amendments to the claims before examination of the application is respectfully requested. The claims have been amended for the sake of clarity. No new matter has been added by these amendments. Applicants authorize the Commissioner to charge any required fees to the Deposit Account No. 06-2375, from which the undersigned is authorized to draw.

Respectfully submitted,

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